Upgraded Cobas TaqMan version 2: hidden consequences at cohort level

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Abstract: The viral load quantification constitutes a cornerstone of antiretroviral therapy management. After the switch from the Cobas Ampliprep Amplicor HIV-1 Monitor Test, v. 1,5 (CAP/CA) (Roche Diagnostics, Mannheim, Germany) to CTM2 in August 2009 at the HIV department of the General Hospital in Vienna, multiple internal reports accumulated concerning an increase of detectable HIV-1 viral loads in patients with previous long-term virological suppression. In order to evaluate these observations and their clinical consequences, a retrospective analysis of the number of elevated VL measurements in formerly virological suppressed patients during the first year of CTM2 use was performed. Furthermore, we monitored for consecutive numbers of repeated VL measurements, genotypic testing and for changes of antiretroviral therapy (ART). We recruited 373 of 2078 patients meeting the chosen inclusion criteria (Initiation of ART prior to August 6, 2008; 1 VL measurement in the pre-CTM2 period from August 6, 2008 to August 5, 2009, all VL measurements below the limit of quantification as defined by applied nucleic acid quantification assay (CAP/CA with<50 copies/mL); 1 VL measurement during the CTM2 period from August 6, 2009 to August 5, 2010). 221 (59.2%) remained with an undetectable HIV-1 viral load after implementation of CTM2, whereas 152 (40.8%) became detectable. The newly detected viremia showed a clear increase at the lower end of the dynamic range of quantification by CTM2. Among our 152 patients, 111 (73.0%) had viral loads ranging from 20-200 copies/mL, 6 (4.0%) between 201-400 copies/mL, while 35 (23.0%) patients showed viral loads measurements above>400 copies/mL. Of these newly detectable patients, 132 had a VL repeat and 72 became undetectable, the remaining 60 patients remained detectable. Remarkably, it was striking to find that in the group of patients who when switching to CTM2 reached at once viral loads exceeding 400 copies/mL, 48.3% became undetectable after viral load repeat using again CTM2, suggesting a high test variability at low detection limit but also beyond. Three genotypic resistance testings were performed and 16 patients underwent subsequent ART changes. In summary, the transition to CTM2 was followed by a dramatic increase of detectable viral loads in patients with stable ART and prior virological suppression, which at least in part could not be reproduced in repeat measurements.

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Upgraded Cobas TaqMan version 2: hidden consequences at cohort level

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The viral load quantification constitutes a cornerstone of antiretroviral therapy management. After the switch from the Cobas Ampliprep Amplicor HIV-1 Monitor Test, v. 1,5 (CAP/CA) (Roche Diagnostics, Mannheim, Germany) to CTM2 in August 2009 at the HIV department of the General Hospital in Vienna, multiple internal reports accumulated concerning an increase of detectable HIV-1 viral loads in patients with previous long-term virological suppression. In order to evaluate these observations and their clinical consequences, a retrospective analysis of the number of elevated VL measurements in formerly virological suppressed patients during the first year of CTM2 use was performed. Furthermore, we monitored for consecutive numbers of repeated VL measurements, genotypic testing and for changes of antiretroviral therapy (ART). We recruited 373 of 2078 patients meeting the chosen inclusion criteria (Initiation of ART prior to August 6, 2008; $\geq$1 VL measurement in the pre-CTM2 period from August 6, 2008 to August 5, 2009, all VL measurements below the limit of quantification as defined by applied nucleic acid quantification assay (CAP/CA with $<$50 copies/mL); $\geq$1 VL measurement during the CTM2 period from August 6, 2009 to August 5, 2010). 221 (59.2%) remained with an undetectable HIV-1 viral load after implementation of CTM2, whereas 152 (40.8%) became detectable. The newly detected viremia showed a clear increase at the lower end of the dynamic range of quantification by CTM2. Among our 152 patients, 111 (73.0%) had viral loads ranging from 20–200 copies/mL, 6 (4.0%) between 201–400 copies/mL, while 35 (23.0%) patients showed viral loads measurements above $>$400 copies/mL. Of these newly detectable patients, 132 had a VL repeat and 72 became undetectable, the remaining 60 patients remained detectable. Remarkably, it was striking to find that in the group of patients who when switching to CTM2 reached at once viral loads exceeding 400 copies/mL, 48.3% became undetectable after viral load repeat using again CTM2, suggesting a high test variability at low detection limit but also beyond. Three genotypic resistance testings were performed and 16 patients underwent subsequent ART changes. In summary, the transition to CTM2 was followed by a dramatic increase of detectable viral loads in patients with stable ART and prior virological suppression, which at least in part could not be reproduced in repeat measurements.

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